WHAT IS CLAIMED:

1. A recombinant chimer hepatitis B core (HBc) protein molecule up to about 515 amino acid residues in length that

(a) contains an HBc sequence of at least about 125 of the N-terminal 150 amino acid residues of the HBc molecule that includes (i) the HBc sequence of residue positions 4 through about 75 and about 85 through about 140, (ii) a peptide-bonded heterologous immunogenic epitope at one or more of the N-terminus, in the HBc immunodominant loop or the C-terminus of the chimer, or (iii) a heterologous linker residue for a conjugated epitope present in the HBc immunodominant loop,

(b) contains one to three cysteine residues at an amino acid position of the chimer molecule corresponding to amino acid position -20 to about +1 from the N-terminus of the HBc sequence of SEQ ID NO:247 [N-terminal cysteine residue(s)] in a sequence other than that of the HBc precore sequence and zero to about three cysteine residues toward the C-terminus of the molecule from the C-terminal residue of the HBc sequence and within about 30 residues from the C-terminus of the chimer molecule [C-terminal cysteine residue(s)],

said chimer molecule (i) containing no more than 20 percent conservatively substituted amino acid residues in the HBc sequence, (ii) self-assembling into particles that are substantially free of binding to nucleic acids on expression in a host cell, and said particles being more stable than are particles formed from otherwise identical HBc chimer molecules

that are free of any above-mentioned C-terminal cysteine residue(s) and (i) lack the N-terminal cysteine residue(s) or (ii) in which an N-terminal cysteine residue(s) present in a contemplated chimer molecule is(are) replaced by another residue.

2. The recombinant HBc chimer protein molecule according to claim 1 wherein said peptide-bonded heterologous immunogenic epitope or a heterologous linker residue for a conjugated epitope is a heterologous immunogenic epitope.

3. The recombinant HBc chimer protein molecule according to claim 2 wherein said heterologous immunogenic epitope is a B cell epitope.

4. The recombinant HBc chimer protein molecule according to claim 3 that contains a second heterologous immunogenic epitope peptide-bonded to the N-terminus, in the HBc immunodominant loop or to the C-terminus of the chimer at a position different from that to which the first-named immunogenic epitope was bonded.

5. The recombinant HBc chimer protein molecule according to claim 3 wherein said B cell epitope is peptide-bonded at a position in the HBc sequence between amino acid residues 76 and 85, and at least 5 residues of the HBc sequence of positions 76 to 85 are present.

6. The recombinant HBc chimer protein molecule according to claim 5 wherein the HBc

sequence between amino acid residues 76 and 85 is present, but interrupted by said B cell epitope.

7. The recombinant HBc chimer protein molecule according to claim 2 further including a peptide-bonded immunogenic heterologous T cell epitope peptide-bonded to the N-terminus, in the HBc immunodominant loop or to the C-terminus of the chimer at a position different from that to which the first-named immunogenic epitope was bonded.

8. The recombinant HBc chimer protein molecule according to claim 7 wherein said T cell immunogenic epitope is peptide-bonded to the C-terminal HBc amino acid residue.

9. The recombinant HBc chimer protein molecule according to claim 8 wherein at least one of said C-terminal cysteine residue(s) is present.

10. The recombinant HBc chimer protein molecule according to claim 1 wherein said chimer contains the uninterrupted HBc amino acid residue sequence of position 4 through at least position 140, plus a cysteine residue at the N-terminus of the HBc chimer protein molecule.

11. The recombinant HBc chimer protein molecule according to claim 10 wherein said chimer contains the uninterrupted HBc amino acid residue sequence of position 4 through position 149.

12. The recombinant HBc chimer protein molecule according to claim 1 wherein said chimer

contains a heterologous linker residue for a conjugated epitope present in the HBc immunodominant loop.

13. The recombinant HBc chimer protein molecule according to claim 12 wherein said heterologous linker residue for a conjugated epitope is peptide-bonded at a position in the HBc sequence between amino acid residues 76 and 85, and at least 4 residues of the HBc sequence of positions 76 to 85 are present.

14. The recombinant HBc chimer protein molecule according to claim 13 wherein the HBc sequence between amino acid residues 76 and 85 is present, but interrupted by said heterologous linker residue for a conjugated epitope.

15. The recombinant HBc chimer protein molecule according to claim 14 that contains the HBc amino acid residue sequence of position 4 through at least position 140.

16. The recombinant HBc chimer protein molecule according to claim 15 wherein said chimer contains the HBc amino acid residue sequence of position 4 through position 149.

17. The recombinant HBc chimer protein molecule according to claim 16 wherein said heterologous linker residue for a conjugated epitope is selected from the group consisting of a lysine, aspartic acid, glutamic acid, cysteine and a tyrosine residue.

18. A recombinant hepatitis B virus core (HBc) protein chimer molecule with a length of about 135 to about 515 amino acid residues that contains four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

(a) Domain I comprises about 71 to about 110 amino acid residues whose sequence includes (i) at least the sequence of the residues of position 5 through position 75 of HBc, (ii) one to three cysteine residues at an amino acid position of the chimer molecule corresponding to amino acid position -20 to about +1 from the N-terminus of the HBc sequence of SEQ ID NO:1 [N-terminal cysteine residue(s)] in a sequence other than that of the HBc precore sequence, and (iii) an optional heterologous immunogenic epitope containing up to about 30 amino acid residues peptide-bonded to one of HBc residues 2-4;

(b) Domain II comprises about 5 to about 250 amino acid residues peptide-bonded to HBc residue 75 of Domain I in which (i) zero to all residues in the sequence of HBc positions 76 to 85 are present peptide-bonded to (ii) an optionally present sequence of one to about 245 amino acid residues that are heterologous to HBc and constitute a heterologous immunogenic epitope or a heterologous linker residue for a conjugated epitope;

(c) Domain III is an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and

d) Domain IV comprises (i) five through fourteen residues of an HBc amino acid residue

sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, (ii) zero to three cysteine residues [C-terminal cysteine residue(s)] within about 30 residues from the C-terminus of the chimer molecule, and (iii) zero to about 100 amino acid residues in an immunogenic sequence heterologous to HBc from position 150 to the C-terminus,

said chimer molecule (i) having an amino acid residue sequence in which no more than about 10 percent of the amino acid residues are substituted in the HBc sequence of the chimer and (ii) self-assembling into particles on expression in a host cell, said particles being substantially free of binding to nucleic acids and being more stable than are particles formed from otherwise identical HBc chimer molecules that are free of any above-mentioned C-terminal cysteine residue(s) and (i) lack the N-terminal cysteine residue(s) or (ii) in which an N-terminal cysteine residue(s) present in a contemplated chimer molecule is(are) replaced by another residue.

19. The recombinant HBc chimer protein molecule according to claim 18 that contains two heterologous immunogenic epitopes.

20. The recombinant HBc chimer protein molecule according to claim 19 wherein said two heterologous immunogenic epitopes are present in Domains I and II, II and IV or I and IV.

21. The recombinant HBc chimer protein molecule according to claim 19 wherein one of said

two heterologous immunogenic epitopes is a B cell epitope.

22. The recombinant HBc chimer protein molecule according to claim 19 wherein one of said two heterologous immunogenic epitopes is a T cell epitope.

23. The recombinant HBc chimer protein molecule according to claim 19 wherein one of said two heterologous epitopes is a B cell epitope and the other is a T cell epitope.

24. The recombinant HBc chimer protein molecule according to claim 18 wherein said Domain I includes a heterologous immunogenic epitope peptide-bonded to one of HBc residues 2-4 and said heterologous epitope is a B cell epitope.

25. The recombinant HBc chimer protein molecule according to claim 18 wherein Domain II contains a heterologous immunogenic epitope and said heterologous epitope is a B cell epitope.

26. The recombinant HBc chimer protein molecule according to claim 18 wherein said sequence heterologous to HBc from position 150 to the C-terminus is an immunogenic T cell epitope peptide-bonded to one of HBc residues 140-149.

27. The recombinant HBc chimer protein molecule according to claim 18 wherein Domain II contains a heterologous linker residue for a conjugated epitope.

28. The recombinant HBc chimer protein molecule according to claim 24 that contains one to three C-terminal cysteine residue(s) within about 30 residues of the C-terminus of the chimer molecule.

29. The recombinant HBc chimer protein molecule according to claim 28 that contains a heterologous immunogenic epitope present in Domain II that is a B cell epitope.

30. The recombinant HBc chimer protein molecule according to claim 29 wherein said B cell epitope contains 6 to about 50 amino acid residues.

31. The recombinant HBc chimer protein molecule according to claim 29 wherein said B cell epitope contains 20 to about 30 amino acid residues.

32. The recombinant HBc chimer protein molecule according to claim 28 that contains 1 cysteine residue within about 30 residues from the C-terminus of the chimer molecule.

33. The recombinant HBc chimer protein molecule according to claim 28 wherein the HBc sequence between amino acid residues 76 and 85 is present, but interrupted by said heterologous immunogenic epitope.

34. The recombinant HBc chimer protein molecule according to claim 32 wherein said cysteine residue is located within about five amino acid

residues of the C-terminus of the chimer protein molecule.

35. The recombinant HBc chimer protein molecule according to claim 18 wherein said sequence heterologous to HBc from position 150 to the C-terminus is an immunogenic T cell epitope peptide-bonded to one of HBc residues 140-149.

36. The recombinant HBc chimer protein molecule according to claim 18 wherein said heterologous linker residue for a conjugated epitope or a heterologous epitope is a heterologous linker residue for a conjugated epitope.

37. The recombinant HBc chimer protein molecule according to claim 36 wherein said heterologous linker residue for a conjugated epitope is selected from the group consisting of a lysine, aspartic acid, glutamic acid, cysteine and a tyrosine residue.

38. The recombinant HBc chimer protein molecule according to claim 37 that contains a single cysteine residue at the C-terminus of the HBc chimer protein molecule.

39. A recombinant hepatitis B virus core (HBc) protein chimer molecule with a length of about 170 to about 250 amino acid residues that contains four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

(a) Domain I comprises about the sequence of the residues of position 4 through position 75 of HBc as well as a sequence of up to about 25 residues that contains a cysteine residue at an amino acid position of the chimer molecule corresponding to amino acid position -14 to about +1 from the N-terminus of the HBc sequence of SEQ ID NO:1 [N-terminal cysteine residue];

(b) Domain II comprises about 5 to about 55 amino acid residues peptide-bonded to HBc residue 75 of Domain I in which at least 4 residues in a sequence of HBc positions 76 to 85 are present peptide-bonded to 6 to about 50 amino acid residues that are heterologous to HBc and constitute a heterologous immunogenic epitope;

(c) Domain III is an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and

d) Domain IV comprises (i) 5 through fourteen residues of a HBc amino acid residue sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, (ii) zero or one cysteine residue [C-terminal cysteine residue] within about 30 residues of the C-terminus of the chimer molecule, and (iii) zero to about 50 amino acid residues in an immunogenic sequence heterologous to HBc from position 150 to the C-terminus,

said chimer self-assembling into particles on expression in a host cell, said particles exhibiting a ratio of absorbance at 280 nm to 260 nm of about 1.2 to about 1.6 and being more stable than are particles formed from an otherwise identical HBc chimer molecule that lacks said N-terminal cysteine

residue or in which a N-terminal cysteine residue present in the chimer molecule is replaced by another residue, and having an amino acid residue sequence in which no more than about 5 percent of the amino acid residues are substituted in the HBc sequence of the chimer.

40. The recombinant HBc chimer protein molecule according to claim 39 wherein said heterologous immunogenic epitope of Domain II is a B cell epitope.

41. The recombinant HBc chimer protein molecule according to claim 40 wherein said heterologous immunogenic epitope contains 15 to about 50 amino acid residues.

42. The recombinant HBc chimer protein molecule according to claim 40 wherein said heterologous immunogenic epitope contains 20 to about 30 amino acid residues.

43. The recombinant HBc chimer protein molecule according to claim 40 wherein the HBc sequence between amino acid residues 76 and 85 is present, but interrupted by said heterologous immunogenic epitope.

44. The recombinant HBc chimer protein molecule according to claim 40 wherein said B cell epitope is an amino acid sequence present in a pathogen selected from the group consisting of *Streptococcus pneumonia, Cryptosporidium parvum,* HIV, foot-and-mouth disease virus, influenza virus,

Yersinia pestis, Haemophilus influenzae, Moraxella catarrhalis, Porphyromonas gingivalis, Trypanosoma cruzi, Plasmodium falciparum, Plasmodium vivax, Plasmodium berghi, Plasmodium yoelli, Streptococcus sobrinus, Shigella flexneri, RSV, *Plasmodium Entamoeba histolytica, Schistosoma japonicum, Schistosoma mansoni,* bovine inhibin and ebola virus.

45. The recombinant HBc chimer protein molecule according to claim 40 wherein said sequence heterologous to HBc from position 150 to the C-terminus is an immunogenic T cell epitope peptide-bonded to one of HBc residues 140-149.

46. The recombinant HBc chimer protein molecule according to claim 45 wherein said T cell epitope is from the organism against which a contemplated chimer is to be used as an immunogen.

47. The recombinant HBc chimer protein molecule according to claim 40 wherein said N-terminal cysteine residue is located within about five amino acid residues of the N-terminal of the chimer protein molecule.

48. An immunogenic particle comprised of recombinant hepatitis B core (HBc) chimeric protein molecules, said chimeric protein molecules being up to about 515 amino acid residues in length and

(a) containing an HBc sequence of at least about 125 of the N-terminal 150 amino acid residues of the HBc molecule that includes (i) the HBc sequence of residue positions 4 through about 75 and about 85 through about 140, (ii) a peptide-bonded

heterologous immunogenic epitope at one or more of the N-terminus, in the HBc immunodominant loop and the C-terminus of the chimer, or (iii) a heterologous linker residue for a conjugated epitope present in the HBc immunodominant loop,

(b) containing one to three cysteine residues at an amino acid position of the chimer molecule corresponding to amino acid position -20 to about +1 from the N-terminus of the HBc sequence of SEQ ID NO:1 [N-terminal cysteine residue(s)] in a sequence other than that of the HBc precore sequence and zero to about three cysteine residues toward the C-terminus of the molecule from the C-terminal residue of the HBc sequence and within about 30 residues from the C-terminus of the chimer molecule [C-terminal cysteine residue(s)],

said chimer molecule (i) containing no more than 20 percent conservatively substituted amino acid residues in the HBc sequence, (ii) self-assembling into particles that are substantially free of binding to nucleic acids on expression in a host cell, and

said particles being more stable than are particles formed from otherwise identical HBc chimer molecules that are free of any above-mentioned C-terminal cysteine residue(s) and (i) lack the N-terminal cysteine residue(s) or (ii) in which an N-terminal cysteine residue(s) present in a contemplated chimer molecule is(are) replaced by another residue.

49. The immunogenic particle according to claim 48 that exhibits a 280/260 absorbance ratio of about 1.2 to about 1.7.

50. The immunogenic particle according to claim 48 whose recombinant HBc chimeric protein displays an immunogenic epitope at the N-terminus.

51. The immunogenic particle according to claim 48 whose recombinant HBc chimeric protein displays an immunogenic epitope at the C-terminus.

52. The immunogenic particle according to claim 48 whose recombinant HBc chimeric protein displays a heterologous immunogenic epitope in the immunogenic loop.

53. The immunogenic particle according to claim 48 whose recombinant HBc chimeric protein displays a B cell immunogenic epitope.

54. The immunogenic particle according to claim 48 whose recombinant HBc chimeric protein displays a T cell immunogenic epitope.

55. The immunogenic particle according to claim 48 whose recombinant HBc chimeric protein displays separate B cell and T cell immunogenic epitopes.

56. The immunogenic particle according to claim 48 whose recombinant HBc chimeric protein has a heterologous linker residue for a conjugated epitope in the HBc immunogenic loop.

57. The immunogenic particle according to claim 56 wherein said heterologous linker residue for a conjugated epitope is selected from the group

consisting of a lysine, aspartic acid, glutamic acid, cysteine and a tyrosine residue.

58. The immunogenic particle according to claim 57 wherein said heterologous linker residue for a conjugated epitope is conjugated to a hapten.

59. The immunogenic particle according to claim 58 wherein said hapten is an oligosaccharide.

60. An immunogenic particle comprised of a plurality of recombinant chimeric hepatitis B core (HBc) protein molecules;

said recombinant chimeric HBc protein molecules having a length of about 135 to about 515 amino acid residues that contains four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

(a) Domain I comprises about 71 to about 110 amino acid residues whose sequence includes (i) at least the sequence of the residues of position 5 through position 75 of HBc, (ii) one to three cysteine residues at an amino acid position of the chimer molecule corresponding to amino acid position -20 to about +1 from the N-terminus of the HBc sequence of SEQ ID NO: 1 [N-terminal cysteine residue(s)] in a sequence other than that of the HBc precore sequence, and (iii) an optional heterologous immunogenic epitope containing up to about 30 amino acid residues peptide-bonded to one of HBc residues 2-4;

(b) Domain II comprises about 5 to about 250 amino acid residues peptide-bonded to HBc residue

75 of Domain I in which (i) zero to all residues in the sequence of HBc positions 76 to 85 are present peptide-bonded to (ii) an optionally present sequence of one to about 245 amino acid residues that are heterologous to HBc and constitute a heterologous immunogenic epitope or a heterologous linker residue for a conjugated epitope;

(c) Domain III is an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and

d) Domain IV comprises (i) five through fourteen residues of an HBc amino acid residue sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, (ii) zero to three cysteine residues [C-terminal cysteine residue(s)] within about 30 residues from the C-terminus of the chimer molecule, and (iii) zero to about 100 amino acid residues in an immunogenic sequence heterologous to HBc from position 150 to the C-terminus,

said chimer molecules (i) having an amino acid residue sequence in which no more than about 10 percent of the amino acid residues are substituted in the HBc sequence of the chimer and (ii) self-assembling into particles on expression in a host cell, and

said particles being substantially free of binding to nucleic acids and being more stable than are particles formed from otherwise identical HBc chimer molecules that are free of any above-mentioned C-terminal cysteine residue(s) and (i) lack the N-terminal cysteine residue(s) or (ii) in which an N-terminal cysteine residue(s) present in a

contemplated chimer molecule is(are) replaced by another residue.

61. The immunogenic particle according to claim 60 that exhibit a ratio of absorbance at 280 nm to 260 nm of about 1.4 to about 1.6.

62. The immunogenic particle according to claim 60 wherein the length of said recombinant chimeric HBc protein molecules is about 170 to about 250 amino acid residues.

63. The immunogenic particle according to claim 60 wherein said peptide-bonded heterologous epitope or a heterologous linker residue for a conjugated epitope is a heterologous immunogenic epitope.

64. The immunogenic particle according to claim 63 wherein said heterologous immunogenic epitope is a B cell epitope.

65. The immunogenic particle according to claim 64 that contains a second heterologous epitope peptide-bonded to one of amino acid residues 2-4 of HBc.

66. The immunogenic particle according to claim 65 wherein said B cell epitope is peptide-bonded at a position in the HBc sequence between amino acid residues 76 and 85, and at least 5 residues of the HBc sequence of positions 76 to 85 are present.

67. The immunogenic particle according to claim 66 wherein the HBc sequence between amino acid residues 76 and 85 is present, but interrupted by said B cell epitope.

68. The immunogenic particle according to claim 64 further including a peptide-bonded heterologous T cell epitope.

69. The immunogenic particle according to claim 68 wherein said T cell epitope is peptide-bonded to the C-terminal HBc amino acid residue.

70. A vaccine or inoculum comprising an immunogenic effective amount immunogenic particles according to claim 48 dissolved or dispersed in a pharmaceutically acceptable diluent.

71. The vaccine or inoculum according to claim 70 wherein said recombinant chimeric HBc protein molecule particles are present in plant tissue.

72. The vaccine or inoculum according to claim 70 that further includes an adjuvant.

73. The vaccine or inoculum according to claim 72 wherein said adjuvant is alum.

74. The vaccine or inoculum according to claim 72 wherein said adjuvant is a small molecule selected from the group consisting of a muramyl dipeptide, 7-substituted-8-oxo- or 8-sulfo-guanosine

derivative, monophosphoryl lipid A, aluminum or calcium salts.

75. The vaccine or inoculum according to claim 72 wherein said adjuvant is an oil that is emulsified with said immunogenic particles and said pharmaceutically acceptable diluent.

76. The vaccine or inoculum according to claim 75 wherein said emulsion is an water-in-oil emulsion having a water phase and an oil phase.

77. The vaccine or inoculum according to claim 75 wherein said emulsion is an oil-in-water emulsion having a water phase and an oil phase.

78. The vaccine or inoculum according to claim 77 wherein the oil phase of said emulsion comprises squalene.

79. The vaccine or inoculum according to claim 75 wherein the oil phase of said emulsion comprises squalane.

80. The vaccine or inoculum according to claim 75 wherein the water and oil phases of said emulsion are emulsified by an emulsifying agent that is a sorbitan or mannide C_{12}-C_{24} fatty acid ester.

81. The vaccine or inoculum according to claim 75 wherein said emulsifying agent is a mannide C_{12}-C_{24} fatty acid ester.

82. The vaccine or inoculum according to claim 81 wherein said C_{12}-C_{24} fatty acid of said mannide C_{12}-C_{24} fatty acid ester is oleic acid.

83. A vaccine or inoculum comprising an immunogenic effective amount immunogenic particles according to claim 60 dissolved or dispersed in a pharmaceutically acceptable diluent.

84. A nucleic acid that encodes a recombinant HBc protein molecule according to claim 1, or a variant, analog or complement thereof.

85. A nucleic acid that encodes a recombinant HBc protein molecule according to claim 18, or a variant, analog or complement thereof.

86. A recombinant nucleic acid molecule that comprises a vector operatively linked to a nucleic acid segment defining a gene that encodes a recombinant HBc protein molecule according to claim 1, or a varient, analog or complement thereof, and a promoter suitable for driving the expression of the gene in a compatible host organism.

87. A recombinant nucleic acid molecule that comprises a vector operatively linked to a nucleic acid segment defining a gene that encodes a recombinant HBc protein molecule according to claim 18, or a varient, analog or complement thereof, and a promoter suitable for driving the expression of the gene in a compatible host organism.

88. A host cell transformed with a recombinant nucleic acid molecule according to claim 86.

89. The transformed host cell according to claim 88 wherein said host cell is selected from the group consisting of *E. coli*, *S. typhi*, *S. typhimurium* and a *S. typhimurium-E. coli* hybrid.

90. A host cell transformed with a recombinant nucleic acid molecule according to claim 87.

91. The transformed host cell according to claim 90 wherein said host cell is selected from the group consisting of *E. coli*, *S. typhi*, *S. typhimurium* and a *S. typhimurium-E. coli* hybrid.

92. A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 70, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.

93. A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 83, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.